Supplementary Material of the article:

Dias, E. P. S., Coelho, A. A., Jacintho, J. C., Brachmann, J. E., Cornélio, B. T., Santos, A. N., & Kipnis, A. (2025). An outreach and academy experience using a synthetic biology approach to aid xeroderma pigmentosum treatment. *Revista Brasileira de Extensão Universitária*, 16(2), 253-267.

Supplementary material 1

Bibliographical research to define the solution

The literature search described below was carried out in the first half of 2023 and revised in July 2024. Its objective is to describe the main findings regarding therapeutic solutions for Xeroderma pigmentosum (XP) already described in the literature. Different search filters were applied during the research to obtain more niche results to describe XP treatments, their methods and technologies.

The literature review process regarding the main existing therapeutic approaches for XP was carried out and approximately 682 works were initially obtained, namely:

- 3 books and documents
- 107 case reports
- 17 clinical studies
- 14 clinical trials
- 1 comment
- 38 comparative studies
- 1 congress
- 1 corrected and republished article
- 26 English abstracts
- 3 evaluation studies
- 1 historical article
- 1 lecture
- 3 letters
- 4 Meta-Analysis
- 1 multicenter study
- 1 preprint
- 41 Research Support, N.I.H., Extramural
- 1 Research Support, N.I.H., Intramural
- 212 Research Support, Non-U.S. Gov't
- 35 Research Support, U.S. Gov't
- 2 randomized controlled trials
- 38 reviews
- 1 systematic review
- 147 without classification

This result was related to the combination of keywords “Xeroderma pigmentosum” and “treatment” and did not exclude any type of article and did not establish publication date limitations. Keywords should be in the title or summary of publications. To obtain results that described treatment solutions for XP, we restricted our search to articles classified as: books and documents, Clinical Trial, Comparative Study, English Abstract, Evaluation Study, Historical Article, Meta-Analysis, Multicenter Study, Randomized Controlled Trial, Research Support, N.I.H., Extramural, Research Support, N.I.H., Intramural, Research Support, Non-U.S. Gov't and Research Support, U.S. Gov't, all open access (totaling 329 works). We then limited the results to the last 15 years (2009 - 2024) and performed a manual analysis to exclude work that did not focus on therapeutics and/or XP. With this filtering, 129 articles published between 2009 and 2024 were included. After manual filtering, we selected 39 works that specifically addressed XP therapeutics for inclusion in the review. The selected articles can be accessed in the table below:

List of articles included in the literature review about existing methodologies for the treatment of XP

Article	Publication year	doi
Clinical trial on the efficacy and safety of NPC-15 for patients with xeroderma pigmentosum exaggerated sunburn reaction type: XP-1 study protocol for a multicentre, double-blinded, placebo-controlled, two-group crossover study followed by a long-term open study in Japan	2023	https://10.1136/bmjopen-2022-068112
XPA Enhances Temozolomide Resistance of Glioblastoma Cells by Promoting Nucleotide Excision Repair	2022	https://10.1177/09636897221092778
Tailoring Supramolecular Prodrug Nanoassemblies for Reactive Nitrogen Species-Potentiated Chemotherapy of Liver Cancer	2021	https://10.1021/acsnano.1c00698
Deubiquitinase PSMD7 promotes the proliferation, invasion, and cisplatin resistance of gastric cancer cells by stabilizing RAD23B	2021	https://10.7150/ijbs.61128
Increased H2O2 levels and p53 stabilization lead to mitochondrial dysfunction in XPC-deficient cells	2021	https://10.1093/carcin/bgab079
NF-κB-induced R-loop accumulation and DNA damage select for nucleotide excision repair deficiencies in adult T cell leukemia	2021	https://10.1073/pnas.2005568118
Spironolactone-induced XPB degradation requires TFIIH integrity and ubiquitin-selective segregase VCP/p97	2021	https://10.1080/15384101.2020.1860559
Oroxylin A reverses hypoxia-induced cisplatin resistance through inhibiting HIF-1α mediated XPC transcription	2020	https://10.1038/s41388-020-

		01474-x
Spironolactone and XPB: An Old Drug with a New Molecular Target	2020	https://10.3390/biom10050756
Loss of Epidermal HIF-1α Blocks UVB-Induced Tumorigenesis by Affecting DNA Repair Capacity and Oxidative Stress	2019	http://10.1016/j.jid.2019.01.035
TGF beta promotes repair of bulky DNA damage through increased ERCC1/XPF and ERCC1/XPA interaction	2019	http://10.1093/carcin/bgy156
Tyrosine kinase receptor TIE-1 mediates platinum resistance by promoting nucleotide excision repair in ovarian cancer	2018	http://10.1038/s41598-018-31069-2
Pembrolizumab treatment of a patient with xeroderma pigmentosum with disseminated melanoma and multiple nonmelanoma skin cancers	2018	http://10.1111/bjd.16525
Spironolactone-induced degradation of the TFIIH core complex XPB subunit suppresses NF-κB and AP-1 signalling	2018	http://10.1093/cvr/cvx198
An endogenous DNA adduct as a prognostic biomarker for hepatocarcinogenesis and its prevention by Theaphenon E in mice	2018	http://10.1002/hep.29380
Xpg limits the expansion of haematopoietic stem and progenitor cells after ionising radiation	2016	http://10.1093/nar/gkw376
New design of nucleotide excision repair (NER) inhibitors for combination cancer therapy	2016	http://10.1016/j.jmgm.2016.02.010
Silibinin enhances the repair of ultraviolet B-induced DNA damage by activating p53-dependent nucleotide excision repair mechanism in human dermal fibroblasts	2015	http://10.18632/oncotarget.5519
Protective Effect of Diphlorethohydroxycarmalol against Ultraviolet B Radiation-Induced DNA Damage by Inducing the Nucleotide Excision Repair System in HaCaT Human Keratinocytes	2015	http://10.3390/md13095629
Phloroglucinol enhances the repair of UVB radiation-induced DNA damage via promotion of the nucleotide excision repair system in vitro and in vivo	2015	http://10.1016/j.dnarep.2015.02.019
Readthrough of stop codons by use of aminoglycosides in cells from xeroderma pigmentosum group C patients	2015	http://10.1111/exd.12655
Pellagra-like condition is xeroderma pigmentosum/Cockayne syndrome complex and niacin confers clinical benefit	2015	http://10.1111/cge.12325
Role of ERCC1 variants in response to chemotherapy and clinical outcome of advanced non-small cell lung cancer	2014	http://10.1111/php.12385
Targeted gene therapy of xeroderma pigmentosum cells using meganuclease and TALEN™	2013	https://doi.org/10.1371/journal.pone.0078678
Repair of UV photolesions in xeroderma pigmentosum group C	2013	http://10.1073/p

cells induced by translational readthrough of premature termination codons		nas.1312088110
Genetic correction of stem cells in the treatment of inherited diseases and focus on xeroderma pigmentosum	2013	http://10.3390/ijms141020019
Kinesin-5: cross-bridging mechanism to targeted clinical therapy	2013	http://10.1016/j.gene.2013.08.004
Role of AMPK in UVB-induced DNA damage repair and growth control	2013	http://10.1038/onc.2012.279
Germline polymorphisms in patients with advanced nonsmall cell lung cancer receiving first-line platinum-gemcitabine chemotherapy: a prospective clinical study	2012	http://10.1002/cncr.26562
Imiquimod-induced TLR7 signaling enhances repair of DNA damage induced by ultraviolet light in bone marrow-derived cells	2011	http://10.4049/jimmunol.1100755
Silymarin protects epidermal keratinocytes from ultraviolet radiation-induced apoptosis and DNA damage by nucleotide excision repair mechanism	2011	http://10.1371/journal.pone.0021410
Radiotherapy for cutaneous cancers with xeroderma pigmentosum	2011	http://10.1016/j.canrad.2011.02.007
Predictive impact of DNA repair functionality on clinical outcome of advanced sarcoma patients treated with trabectedin: a retrospective multicentric study	2011	http://10.1016/j.ejca.2011.01.016
Multiple roles of the ERCC1-XPF endonuclease in DNA repair and resistance to anticancer drugs	2010	https://pubmed.ncbi.nlm.nih.gov/20944091/
Contribution of the cryosurgery in the management of xeroderma pigmentosum	2010	http://10.1016/j.annder.2010.06.029
Lack of influence of XRCC1 and XPD gene polymorphisms on outcome of platinum-based chemotherapy for advanced non small cell lung cancers	2009	https://pubmed.ncbi.nlm.nih.gov/20104979/
Very low prevalence of XPD K751Q polymorphism and its association with XPD expression and outcomes of FOLFOX-4 treatment in Asian patients with colorectal carcinoma	2009	http://10.1111/j.1349-7006.2009.01186.x
The role of Bcl-x(L) protein in nucleotide excision repair-facilitated cell protection against cisplatin-induced apoptosis	2009	http://10.1089/dna.2008.0815
Xeroderma pigmentosum: radical therapeutic procedure on the face using artificial skin	2009	http://10.1016/j.anplas.2008.11.002

Supplementary material 2

Ararasun scientific approach

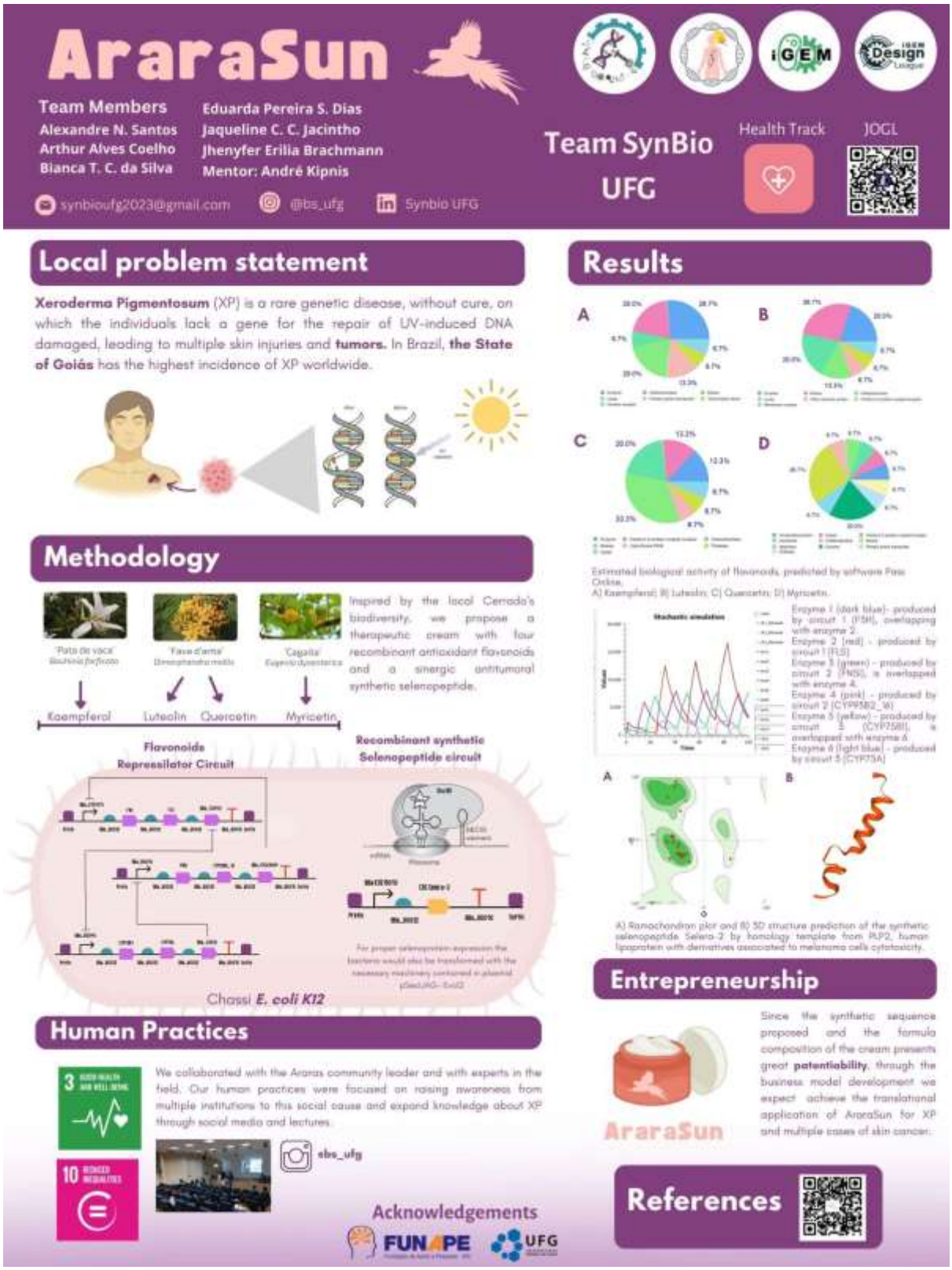
Bioinformatics tools were used to create and develop the scientific project (Supplementary material 2). These steps will not be covered in depth in this article but can be accessed in more detail on the JOGL platform (SynBio UFG, 2023). The choice of the chassis or microorganism to be used for genetic manipulations was a relevant activity in the scientific aspect of the project, which involved researching classic and recent literature on the subject, as well as the choice of flavonoids that were explored in the projects and the trees that produce them and the synthetic peptide. Even though it was a completely theoretical work, ethical issues were taken into consideration by reporting, via form, the objectives of using a given microorganism and what final product we hoped to obtain when genetically manipulating it, what level of safety it met, if the development of the project in some way posed risks to animals and the environment, if the biological parts - Biobricks - posed risks and if we obtained laboratory infrastructure and professionals connected to our educational institution to carry out the steps involved in the project safely. Computational biology tools were also used in this study to develop the scientific aspect of the project. Due to the AraraSun project being developed in the iGEM Design League competition in a completely theoretical way, the use of computational tools was essential to obtain the results. The choice to use each program was based on articles that had similar development objectives concerning AraraSun.

As a result of the use of bioinformatics tools, genetic circuits were built, genes of interest were optimized for expression in bacteria and mathematical modeling of the circuits and the bioreactor were made, allowing students to open horizons concerning computational biology, thus as exposed by Kelwick et al. (2015). The SynBio UFG team generated 14 new biobricks - iDLBB_004240, iDLBB_004241, iDLBB_004242, iDLBB_004243, iDLBB_004244, iDLBB_004245, iDLBB_004246, iDLBB_004247, iDLBB_004248, iDLBB_004249, iDLBB_004250, iDLBB_004251, iDLBB_004252, iDLBB_004253 and iDLBB_004254 - accessible to different research groups once the data bank is open and, consequently, contributes to the generation of new knowledge, new research and even new products (Morales et al., 2022). One of the objectives when establishing extension projects is the exchange and generation of new knowledge (Donaldson, 2020), which we were encouraged and able to generate for the scientific community during the extension project.

Computational biology tools used for Ararasun development

Bioinformatics tools and databases	Description
1. Benchling	A cloud-based platform that displays several tools for biological systems engineering such as recombinant genetic circuit designs, codon optimization, plasmids construction, and validation of assemble methods.
2. KEEG	A biological database that disposes information on biological molecules interaction such as systems in biology, including metabolic and biochemical routes, enzymes, and flavonoids.
3. PassOnline	An open software for biological activity prediction of chemical compounds, including pharmacological effects, mechanism of action, toxicity and adverse effects.
4. TinkerCell	A web-based tool that allows the design of plasmids, genetic networks and artificial systems based on standard genetic parts. This tool also can be used to predict the gene expression of artificial genetic circuits.
5. PepDraw	An online open tool to draw peptide primary structure and calculate theoretical properties.
6. SwissModel	An open web server for protein 3D model prediction based on the method of homology-modelling, using a comparative structural approach.
7. Bioreactor Design 4.0	A web-based program for the design of different kinds of bioreactors, allowing the prediction of parameters such as rotation, gas flow and net yield.

Supplementary Material 3
Arasun poster



Supplementary Material 4

Entrepreneurship and UN Sustainable Development Goals (SDG)

The proposal contributes to the United Nation's (UN) Sustainable Development Goals (SDG), as the business was designed to achieve socio-environmental agendas and have clients that contribute to such impact agendas - companies that work with environmental, social and governmental (ESG) policies. The connection with XP holders, who, even though they are not our direct customers, are the ones who should benefit most and be monitored concerning the use of AraraSun, was also valued. The way to reach customers was designed to be done at events, through health professionals and government officials. The partnership with producers of orange juice and its derivatives is essential so that the raw material - orange peel - for the production of flavonoid synthesis by the recombinant enzyme pathway is committed. Pharmaceutical industries would help us with the research and manufacturing of AraraSun, and non-governmental organizations (NGOs) would contribute to reaching out to XP holders and other people who can benefit from using AraraSun. Key activities and resources focused on the development of AraraSun, its manufacturing and marketing. Additionally, activities focused on the scientific dissemination of information about XP and non-melanoma cancer were planned. These initiatives aimed to educate the community and general public about these issues and potential solutions. Finally, the costs for us to envisage the implementation of the business model were focused on laboratory infrastructure, human resources and sales strategies. To make the business sustainable from a financial point of view, we focus on selling AraraSun units to the previously defined customer segment, combined with public-private partnerships.

SDG 3 was worked on in the project as we researched and theoretically developed a possible solution that mitigates the damage caused by XP. SDG 3, according to the UN report "Science, Technology, and Innovation for the SDGs – Progress, Future Vision, and Recommendations," is the one that receives the most public capital expenditure in research and development, a fact which contributes to the future development of the AraraSun. We also work on goals to reduce inequalities, as populations with rare diseases are generally vulnerable and marginalized (NGO Committee for Rare Diseases, 2024). A solution that mitigates the effects of the disease, combined with increased publicity about it, can contribute to reducing these inequalities. Finally, our proposal contributes to SDG 12, as, in the development of technology, we incorporate techniques for using organic waste (orange peel) and consequently reduce the use of chemical reagents that are harmful to the environment. In this sense, our technology reduces the "material footprint" concerning biomass production (Nature Editorial, 2023).

Supplementary Material 5

SynBio team prizes and nominations

All the awards that the SynBio team was nominated for or won are described in the table below. These awards were obtained through the iGEM Design League 2023 competition, which had 22 participating teams. The teams must be from Latin American countries that could have different themes that were problems in their respective countries.

SynBio UFG prizes and nominations of iDL 2023

Categories	SynBio UFG Team position
Grand Prize	1st RunnerUp (second place)
Best project Human Health & Biomedicine track	Winner
Best project video	Nominated
Best design league poster	Nominated
Best promotional video	Winner
Best design roadmap	Nominated
SDG Impact	Nominated
Best partnership and collaboration	Nominated
Best entrepreneurial approach	Nominated
Vision award	Nominated
Integrated Human Practices	Winner
Local heroes	Winner
Best genetic design circuit	Winner
Best biological engineering excellence	Nominated

Reports

SynBio UFG Wins 2nd Place in International Competition with Revolutionary Therapeutic Cream for Xeroderma Pigmentosum

Evento destaca experiência da UFG em competição de Biologia Sintética

IPTSP IN THE MEDIA - Featured in the O Popular Newspaper!

Alunos da UFG conquistam premiação inédita em Biologia Sintética | O Popular

Equipe da UFG desenvolve projeto de creme para tratar Xeroderma Pigmentoso

UFG desenvolve creme para tratar xeroderma pigmentoso | O Popular